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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/121,798	07/23/98	BRIDENBAUGH	R 018484-00120

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EXAMINER	
SANDALS, W	
ART UNIT	**PAPER NUMBER**
1636	12
DATE MAILED:	09/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

Office Action Summary	Application No. 09/121,798	Applicant(s) Bridenbaugh et al
	Examiner WILLIAM SANDALS	Group Art Unit 1636

☒ Responsive to communication(s) filed on *Jul 5, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-20* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *9*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Arguments

1. Amendments to the specification in Paper No. 11, filed July 5, 2000 has overcome the rejection of claims 1 and 18 under 35 USC 112, second paragraph in the previous office action, and the rejection is withdrawn.

2. Arguments with respect to the rejection of claims 1-20 under 35 USC 103 have been considered but are moot in view of the new ground(s) of rejection.

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 17-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-62 of U.S. Patent No. 6,011,148. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only substantial differences between the claimed invention and that disclosed by US Pat. No. 6,011,148 is the use of static mixers in the plasmid isolation prior to the use of ultrafiltration and or anion exchange chromatography in a plasmid procedure that can be readily automated.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/02658 in view of US Pat No. 5,837,529 and Maniatis, T. (both of record).

The claims are drawn to a method for purifying at least about 100 mg. of plasmid DNA for pharmaceutical use by mixing the DNA and an alkaline lysing agent in a static mixer, then adding a precipitation agent in a second static mixer, removing the precipitated component by centrifugation, neutralizing the solution, and passing the clarified solution over an ion exchange column.

WO 96/02658 taught (see especially the abstract and pages 4, 6 and 8-10 and the claims) a method for purifying at least about 100 mg. of plasmid DNA for pharmaceutical use by mixing the DNA and heat lysing of the cell mass, then adding a precipitation agent, removing the precipitated component by centrifugation, ultrafiltering the solution, and passing the clarified solution over an ion exchange column.

WO 96/02658 did not teach the use of an alkaline lysis agent, neutralizing agent, nor static mixers.

US Pat No. 5,837,529 taught (see the entire patent) the use of an alkaline lysis agent for preparation of plasmids with a neutralizing agent and static mixers.

Maniatis taught the equivalence of heat lysing of the cell mass was equivalent to alkaline lysis of the cell mass in a plasmid purification method.

It would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the method for purifying at least about 100 mg. of plasmid DNA for pharmaceutical use by mixing the DNA and heat lysing of the cell mass, then adding a precipitation agent, removing the precipitated component by centrifugation, ultrafiltering the solution, and passing the clarified solution over an ion exchange column of WO 96/02658 with the use of an alkaline lysis agent for preparation of plasmids with a neutralizing agent and static mixers of US Pat No. 5,837,529 because US Pat No. 5,837,529 taught that the method of use of static mixers provided an advantage in the large scale pharmaceutical production of plasmids

over other methods of mixing, and Maniatis taught the equivalence of heat lysis of WO 96/02658 and the alkaline lysis of US Pat No. 5,837,529.

One of ordinary skill in the art would have been motivated at the time of filing of the instant application to combine the method for purifying at least about 100 mg. of plasmid DNA for pharmaceutical use by mixing the DNA and heat lysing of the cell mass, then adding a precipitation agent, removing the precipitated component by centrifugation, ultrafiltering the solution, and passing the clarified solution over an ion exchange column of WO 96/02658 with the use of an alkaline lysis agent for preparation of plasmids with a neutralizing agent and static mixers of US Pat No. 5,837,529 because US Pat No. 5,837,529 taught at column 2, line 64, bridging to column 3, line 9 "[t]his invention is based upon the discovery that static mixers could be used to lyse cells containing plasmids, releasing the plasmids from the cells. The advantage of using such a device is that large volumes of cells can be gently and continuously lysed in-line using the static mixer and that other static mixers could be place in-line to accomplish other functions such as dilution and precipitation. This method greatly simplifies the process of isolating plasmids from large volumes of material such as plasmid DNA is not damaged by the process. Previous methods of plasmid isolation involving caustic lysing and precipitation, which involved expensive and specialized equipment, were not practical for large scale plasmid purification", and Maniatis taught the equivalence of heat lysis of WO 96/02658 and the alkaline lysis of US Pat No. 5,837,529. Further, a person of ordinary skill in the art would have had a

reasonable expectation of success in the producing the instant claimed invention given the teachings of WO 96/02658 with US Pat No. 5,837,529 and Maniatis, T.

Response to Arguments

8. Arguments set forth in Paper No. 11 assert that US Pat No. 5,837,529 fails to teach a 32 element static mixer, not the (2) 24 element static mixer as claimed in claims 7 and 11.. US Pat No. 5,837,529 taught at column 3, lines 33-36 "[s]uitable static mixers useful in the method of the present invention include any flow through device referred to in the art as a static or motionless mixer of length sufficient to allow the processes of the present invention."

9. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/02658 in view of US Pat No. 5,837,529 and Maniatis, T. above, and further in view of US Pat No. 5,256,294 and US Pat No. 5,034,314.

The claims are drawn to a method described above and for purifying a nucleic acid from a solution by ultrafiltering the solution through an ultrafilter comprising a gel layer which retains the nucleic acid, thereby purifying the nucleic acid. The ultrafilter may be in an open-channel, flat plate or hollow fiber device.

WO 96/02658 in view of US Pat No. 5,837,529 and Maniatis, T. taught a method as described above.

WO 96/02658 in view of US Pat No. 5,837,529 and Maniatis, T. did not teach purifying a nucleic acid from a solution by ultrafiltering the solution through an ultrafilter comprising a gel

layer which retains the nucleic acid, thereby purifying the nucleic acid. The ultrafilter may be in an open-channel, flat plate or hollow fiber device.

US Pat No. 5,256,294 taught (see especially the abstract, columns 2-7, 10 and the examples) that a gel layer is inherent in all ultrafiltration processes. Also taught is that the process can be performed in dead ended, tangential flow (with or without screens) and hollow fiber devices.

US Pat No. 5,034,314 taught (see especially the abstract, summary and examples) practical ranges of operation of a tangential flow ultrafiltration device for purification of DNA.

One of ordinary skill in the art would have been motivated at the time of filing to combine the method for purifying a nucleic acid from a solution by ultrafiltering the solution through an ultrafilter which retains the nucleic acid, thereby purifying the nucleic acid where the ultrafilter may be in an open-channel, flat plate or hollow fiber device where the molecular weight cut-off of the membrane may be from about 50K to 500K daltons where the solution may be diafiltered in the ultrafiltration device where the nucleic acid may be a plasmid, and may be passed over an ion exchange resin and the purified nucleic acid may be in a pharmaceutical composition of WO 96/02658 with the teachings of US Pat No. 5,256,294 regarding the formation of a gel layer in an ultrafilter, or the variables of operation of an ultrafiltration device because US Pat No. 5,256,294 taught the theoretical knowledge of one of skill in the art when using an ultrafiltration device to filter DNA as recited at column 4, lines 36-37 "the polarized layer can never be completely eliminated", and then at lines 60-68 "[i]t is another object to

provide improved filtration processes, including ultrafiltration processes, for separating biological macromolecules such as proteins which processes minimize concentration polarization and do not increase flux. It is another object to provide a filtration process that can separate by size species that are less than ten-fold different in size". US Pat No. 5,034,314 imparts practical knowledge as to the various parameters which can be used to effect separation of nucleic acid species by ultrafiltration. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of WO 96/02658 in view of US Pat No. 5,837,529 and Maniatis, T. an further in view of US Pat No. 5,256,294 and US Pat No. 5,034,314.

Response to Arguments

10. Arguments set forth in Paper No. 11 assert that US Pat No. 5,256,294 did not teach conditions suitable for plasmid purification, nor the use of open-channel devices. US Pat No. 5,256,294 taught that a gel layer was an inherent element in all ultrafiltration, and at column 12 describe open channel devices suitable for use in the method. US Pat No. 5,256,294 taught the use of ultrafiltration in the scheme of the method, US Pat No. 5,034,314 provided the well known suitable conditions for the practice of the method.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

William Sandals, Ph.D.
Examiner
September 17, 2000

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER